REMARKS

The above-identified patent application has been amended and Applicants respectfully request the Examiner to reconsider and again examine the claims as amended.

Claims 1-49 are pending in the application. Claims 1-45 are rejected. Claims 1, 6, 21, 26, and 40 are amended herein. Claims 3-5, 7-9, 10-13, 18, 23-25, 27-30, 32, 33, and 37 are also amended herein, but for clarity and not for reasons of patentability as will be apparent. Claims 42 and 43 are canceled herein without prejudice. Claims 46-49 are new.

The Rejections under 35 U.S.C. §102(b)

In View of Ntziachristos et al.

The Examiner rejects Claims 1-7, 9-11, 13, 19-26, 28-30, 32, 38-39, and 44-45 under 35 U.S.C. §102(b) as being anticipated by Ntziachristos et al. (International Publication number WO 02/041760 A2)

Applicants submit that amended Claims 1 and 21 are is patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "...an apparent light source configured to project excitation light toward a specimen having fluorescent proteins therein, wherein the excitation light enters the specimen becoming intrinsic light within the specimen, wherein the intrinsic light is configured to excite fluorescent light from the fluorescent proteins, and *wherein at least one of the intrinsic light or the fluorescent light has a wavelength in a visible wavelength range and outside of a near infrared range*," as set forth in Claims 1 and 21.

With this particular arrangement, the present invention provides the claimed system suitable for operation using *fluorescent proteins that use visible light outside of a near infrared range*. Support for the claimed arrangement can be found, for example, at page 8 of the

corresponding published PCT application (which is presumed herein to be the specification of this U.S. national stage application), where it is stated:

> While the method and system of the present invention are described herein as applied to fluorescent proteins that emit visible fluorescent light, providing particular benefits in the visible wavelength range of about 400nm to 700nm, the method and system can also be applied to light having other wavelengths, for example to fluorescent light in the near infra red (NIR) range of about 700nm to 1000nm. Also, the method and system apply equally well to a system in which excitation light is in one wavelength range, for example, in the visible range, and the fluorescent light emitted by the fluorescent proteins is in another wavelength range, for example in the NIR range. The method and system also apply where both the excitation light and the fluorescent light emitted by the fluorescent proteins are in the NIR range or both are in the visible range. Also, light beyond the wavelength range of 400nm to 1000nm can be used.

It should be recognized that wavelength boundaries of visible light and of near infrared light are not precisely defined in general. However, a boundary of about 700 nanometers is given above as a boundary between visible and near infra red light. It will also be recognized, as described more fully below, that the Ntziachristos et al. reference discusses a wavelength of 673 nanometers as being near infrared. Nevertheless, it should be clear from the written description of the present patent application that the system and methods described therein are targeted at least at the visible region of the spectrum of light and that Claims 1 and 21 have been amended accordingly.

A system suitable for optical tomography at visible wavelengths of light will be understood to be difficult to achieve. For example, at page 3 of the corresponding published PCT application, it is stated:

> As is known, all currently available fluorescent proteins utilize excitation light having a wavelength in the visible range. Moreover, conventional fluorescent proteins emit visible fluorescent light when excited. Tomographic imaging using visible light, as provided by the conventional fluorescent proteins, is complicated by a relatively high absorption of visible light propagating in biological tissue, which results in significant attenuation. With high absorption, (e.g., for visible light) the conventional diffusion approximation described above is not valid.

Using visible light has particular advantages not achieved when using light having longer wavelengths. For example, at page 28, lines 23-25 of the corresponding published PCT application, it is stated:

> It should be appreciated that the method and system of the present invention, when using visible light, provides higher spatial resolution than conventional tomographic approaches using near-infrared (NIR) light.

In contrast, Ntziachristos et al. provides a system that operates using near infrared (NIR) light (see, e.g., abstract). Ntziachristos et al. describes optical tomography using a variety of fluorescent probes, which are not fluorescent proteins. For example, at page 18, Ntziachristos et al. describes a fluorochrome Cy with an excitation wavelength of 673 nanometers and an emission wavelength of 694 nanometers, which are described to be near infrared wavelengths. Applicants submit that Ntziachristos et al. is concerned only with propagation of near infrared light in tissue, which does not present the same difficulties as propagation of visible light outside of the near infrared range in tissue.

In view of the above, Applicants submit that independent Claims 1 and 21 are patentably distinct over Ntziachristos et al.

Claims 2-7, 9-11, 13, 19, 20, and 44 depend from and thus include the limitations of Claim 1. Thus, Applicants submit that Claims 2-7, 9-11, 13, 19, 20, and 44 are patentably distinct over the cited reference at least for the reasons discussed above in conjunction with Claim 1. Claims 22-26, 28-30, 32, 38-39, and 45 depend from and thus include the limitations of Claim 21. Thus, Applicants submit that Claims 22-26, 28-30, 32, 38-39, and 45 are patentably distinct over the cited reference at least for the reasons discussed above in conjunction with Claim 21.

For reasons discussed above in conjunction with Claims 1 and 21, Applicants submit that Claims 3 and 21 are further patentably distinct over Ntziachristos et al., since the cited reference

neither describes nor suggests "... *the fluorescent light has a wavelength in the visible wavelength range and outside of the near infrared range*," as set forth in Claims 3 and 23.

Applicants submit that Claims 4 and 24 are further patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "... *the fluorescent light has a wavelength in a red portion of the visible wavelength range*," as set forth in Claims 4 and 24. The Examiner uses the Cy 5.5 fluorochrome of Ntziachristos et al., which has an emission wavelength of about 694 nanometers, to teach the red portion of a visible wavelength range. However, at page 18, Ntziachristos et al. describes 694 nanometers to be within a near infrared range, not within a red range as claimed.

For reasons discussed above in conjunction with Claim 1 and 21, Applicants submit that Claim 6 is further patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "...an image processor coupled to the light detector and configured to generate a light propagation model, *wherein the light propagation model is configured to predict propagation of visible light in a diffuse medium*, wherein the image processor is further configured to combine the first image information, the second image information, and the light propagation model, and further configured to provide a tomographic image of the fluorescent proteins, wherein *the light propagation model is configured to predict the propagation of the visible light in the visible wavelength range and outside of the near infrared range*," as set forth in Claim 6.

For reasons discussed above in conjunction with Claims 1 and 21, Applicants submit that Claim 7 is further patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "...*the image processor includes a diffusion equation processor that uses a diffusion equation having a modified diffusion coefficient selected in accordance with the propagation of the visible light and associated with at least one of the intrinsic light or the fluorescent light*," as set forth in Claim 7.

For reasons discussed above in conjunction with Claim 1 and 21, Applicants submit that Claim 26 is further patentably distinct over Ntziachristos et al., since the cited reference neither describes nor suggests "...*using a light propagation model configured to predict propagation of the visible light in a diffuse medium, wherein the light propagation model is configured to predict the propagation of visible light having a wavelength in the visible wavelength range and outside of the near infrared range*... ," as set forth in Claim 26.

In view of the above, Applicants submit that the rejection of Claims 1-7, 9-11, 13, 19-26, 28-30, 32, 38-39, and 44-45 under 35 U.S.C. §102(b) should be removed.

In View of Takada et al.

The Examiner rejects Claims 40-42 under 35 U.S.C. §102(b) as being anticipated by Takada et al. (European Patent Application number 0 336 208)

Applicants submit that amended Claim 40 is patentably distinct over Takada et al., since the cited reference neither describes nor suggests "...at least one selectively movable component to selectively move a projection direction of the apparent light source to direct a plurality of light paths toward a specimen, *wherein the selectively movable component includes a selectively movable structure comprising an optical fiber, wherein the selectively movable structure is configured to move the optical fiber to a plurality of physical locations to provide the plurality of light paths*," as set forth in Claim 40.

In contrast, in Fig. 5, Takada et al. teaches a moveable reflector 7 to direct light generated by a light source 5 through an object 3.

Claim 41 depends from and thus includes the limitations of Claim 40. Thus, Applicants submit that Claim 41 is patentably distinct over the cited reference at least for the reasons discussed above in conjunction with Claim 40.

As described above, Claims 42 and 43 are canceled herein without prejudice.

In view of the above, Applicants submit that the rejection of Claims 40-43 under 35 U.S.C. §102(b) should be removed.

The Rejections under 35 U.S.C. §103(a)

Ntziachristos et al. in View of Takada et al.

The Examiner rejects Claims 8, 12, 14-18, 27, 31, and 33-37 under 35 U.S.C. §103(a) as being unpatentable over Ntziachristos et al. in view of Takada et al.

Claims 8, 12, and 14-18 depend from and thus include the limitations of Claim 1. Thus, Applicants submit that Claims 8, 12, and 14-18 are patentably distinct over the cited references at least for the reasons discussed above in conjunction with Claim 1. Claims 27, 31, and 33-37 depend from and thus include the limitations of Claim 21. Thus, Applicants submit that Claims 27, 31, and 33-37 are patentably distinct over the cited references at least for the reasons discussed above in conjunction with Claim 21.

Applicants submit that Claim 8 is further patentably distinct over Ntziachristos et al., whether taken alone or in combination with Takada et al., since the cited references neither describe nor suggest "... *the light detector is selectively movable to receive the intrinsic light and fluorescent light on a plurality of light paths relative to the specimen*," as set forth in Claim 8.

With regard to Claims 8, the Examiner recognizes that Ntziachristos et al. "...does not disclose expressly selectively movable detector." The Examiner recognizes that Takada et al. teaches "...a selectively movable stage upon which the specimen is located... ." The Examiner asserts that "...[t]he movement between the light source and the specimen versus that of the detector is a matter of apparent motion in different frames of reference." The Examiner asserts that "[i]t would be a simple matter of design choice for one of ordinary skill in the art at the time

the invention was made to employ a selectively moveable light source, specimen, detector, or any combination thereof." Applicants respectfully disagree.

According to the Federal Register, Volume 72, No. 195, dated October 10, 2007, at page 57528, Part III of the section entitled "Examination Guidelines for Determining Obviousness under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*," an obviousness rejection may be made using the familiar teaching-suggestion-motivation (TSM) rationale... ." In Part III, it is also stated that "[a]lthough the Supreme Court in *KSR* cautioned against an overly rigid application of TSM, it also recognized that TSM is one of a number of valid rationales that could be used to determine obviousness." Thus, as one criteria used to establish prima facie obviousness, there should be some suggestion and motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Applicants respectfully submit that the Examiner has not shown a suggestion or motivation to modify the references or to combine reference teachings.

In particular, since the references teach only moving the apparent light source and moving the specimen, Applicants submit that one of ordinary skill in the art in possession of Ntziachristos et al. and Takada et al., would not be motivated to move the light paths through the specimen by another means, i.e., by moving the light receiver. Applicants submit that the Examiner is merely using hindsight to establish his conclusion of obviousness.

For reasons discussed above in conjunction with Claim 8, Applicants submit that Claim 27 is further patentably distinct over Ntziachristos et al., whether taken alone or in combination with Takada et al., since the cited references neither describe nor suggest "... receiving the intrinsic light and receiving the fluorescent light with *a selectively movable light detector* configured to receive the intrinsic light and fluorescent light on a plurality of light paths relative to the specimen," as set forth in Claim 27.

In view of the above, Applicants submit that the rejection of Claims 8, 12, 14-18, 27, 31, and 33-37 under 35 U.S.C. §103(a) should be removed.

Takada et al. in View of Ntziachristos et al.

The Examiner rejects Claim 43 under 35 U.S.C. §103(a) as being unpatentable over Takada et al. in view of Ntziachristos et al. As described above, Claim 43 is canceled herein without prejudice. Therefore, the rejection of Claim 43 is moot and should be removed.

Claims 46-49 are new in the application. Consideration of new Claims 46-49 is respectfully requested.

In view of the above Amendment and Remarks, Applicants submit that the claims and the entire case are in condition for allowance and should be sent to issue and such action is respectfully requested.

The Examiner is respectfully invited to telephone the undersigning attorney if there are any questions regarding this Amendment or this application.

The Assistant Commissioner is hereby authorized to charge payment of any additional fees associated with this communication or credit any overpayment to Deposit Account No. 500845, including but not limited to, any charges for extensions of time under 37 C.F.R. §1.136.

Respectfully submitted,

Dated: 6 Feb. 2009

DALY, CROWLEY, MOFFORD & DURKEE, LLP

By: _____

Kermit Robinson
Reg. No. 48,734
Attorney for Applicant(s)
354A Turnpike Street - Suite 301A
Canton, MA 02021-2714
Tel.: (781) 401-9988, Ext. 124
Fax: (781) 401-9966
kr@dc-m.com

97985.doc